Sentinel lymph node (SLN) biopsy has rapidly emerged as a minimally invasive and accurate method of axillary staging in patients with early-stage breast cancer and has become the standard of care in many countries worldwide. Unnecessary axillary lymph node dissections can be avoided resulting in fewer complications for patients.

Intra-operative examination of the SLN using conventional cellular pathology methods was introduced to further benefit patients by making one-step surgery a realistic possibility. However, intra-operative methods such as touch imprint cytology or frozen section suffer from a lack of sensitivity and are not standardised, thus providing a considerable number of false negative patient results. A significant number of metastases can only be detected later by more detailed post-operative analysis. These patients in general need to undergo avoidable second surgeries.

Furthermore, recent findings concerning the clinical relevance of metastases in SLNs require a clear picture of the extent of tumour burden and reliable and standardised results for a more accurate staging. Sysmex have created a new diagnostic dimension with the OSNA molecular diagnostic assay. In contrast to the conventional methods, analysis of the complete lymph node with OSNA provides a highly accurate result supporting a final clinical decision even in an intra-operative timeframe.

The quantitative measurement of the CK19 marker not only allows differentiation between a positive and a negative result. It also gives an indication for the size of the metastatic tumour burden. The amplification reaction takes 16 minutes and is monitored in real time. Results are displayed in three categories with a direct relation to the measured copy numbers of CK19 mRNA:

- (++) = macrometastatic tumour burden
- (+) = micrometastatic tumour burden
- (-) = no metastases

The method is also applicable to lymph node analysis of patients after neoadjuvant therapy (PST) for whom a SLNB is indicated.

OSNA is CE-marked and compliant with the in vitro diagnostic directive 98/79/EC. It is thus approved for diagnostic use throughout Europe.

- Fast, intra-operative decision
- Automated and standardised procedure
- Also for patients after PST

**OSNA** (One Step Nucleic Acid Amplification) is an isothermal procedure using a rapid nucleic acid amplification technology (RT-LAMP*) to detect the expression level of Cytokeratin 19 (CK19) mRNA. Cytokeratin 19, an epithelial cell marker, is normally not present in lymph node tissue. Six primers for high levels of specificity and sensitivity have been specifically designed thus allowing the use of a single marker without amplification of pseudogenes. Furthermore false positive results are avoided because the use of an isothermal method prevents amplification of genomic DNA.

Lymph node tissue is simply homogenised and no prior purification of RNA is required. The samples are inserted into the RD-100i automated real time detection system providing fast, accurate and standardised results. Up to 4 lymph nodes can be analysed in parallel and results are available in about 30-40 minutes depending on the number of SLN analysed.

*RT-LAMP = reverse transcriptase loop-mediated isothermal amplification; licensed under the agreement of Eiken Chemical Co., Ltd*
OSNA offers a new standard of care in breast cancer for lymph node testing. Many investigators have reported that intra-operative techniques such as imprint cytology or frozen section have low sensitivity due to the limited amount of lymph node tissue that can be analysed in a short timeframe. False negative rates are significant and, as a consequence, a significant number of patients need to undergo second surgeries after a positive subsequent post-operative examination. On the other hand, patients with very low metastatic nodal involvement, to whom axillary dissection could be spared, can be identified with this test.

For OSNA worldwide evaluations have shown sensitivity and specificity of over 96% in a comparison to extensive post-operative analysis by analysing alternating slices of one lymph node. As a result, many centres are now using OSNA in routine and patients benefit from an immediate and reliable diagnosis. Importantly, the proportion of the lymph node tested can be controlled according to local policy. Under optimum circumstances where whole node analysis is performed and a definite result has been obtained with OSNA, post-operative investigation can be abandoned. This leads to a reduction in work-load and costs as intensive sectioning and IHC* are avoided.

OSNA does not require the expertise of a molecular biologist. The test can be easily implemented in any institution.

- higher sensitivity than conventional intra-operative techniques
- indication for the size of metastatic tumour burden
- automated system, easy to operate
- reduced pathology workload

Rapid detection of sentinel lymph node metastases in breast cancer patients enables an immediate decision to proceed to axillary lymph node dissection, where indicated. This spares patients a second anaesthetic and operative procedure, is technically easier, and decreases psychological stress for many patients. The OSNA result in the form of the CK19 mRNA copy number gives an indication for the size of metastasis in the lymph node and enables prediction of further axillary lymph node involvement. This allows the surgeon to take a differential decision on the appropriate surgical approach and constitutes an additional parameter to facilitate decision making on necessary adjuvant therapy and radiotherapy regimens. Omission of post-operative analysis leads to faster and final therapeutic measures.

- enhanced staging of the patient
- immediate and reliable intra-operative decision
- immediate reconstruction possible
- reduced number of second surgeries
- reduced waiting time and patient stress
- assessment of the axillary status
- earlier start of treatment

* IHC = immunohistochemistry
ONE Patient – ONE Goal

Using OSNA can offer a real competitive advantage for the hospital since breast cancer patients may prefer a hospital using this innovative method. The patients will receive very fast and accurate sentinel lymph node analysis in one step. Therefore they will not need to wait for final post-operative results days after the first surgery with the accompanying risk of being recalled for axillary clearance. Without this waiting time and within a more personalised treatment concept, the psychological pressure on the patient will be reduced and as a result OSNA increases quality of life.

ONE Budget – ONE Aim

In addition to clinical and procedural benefits that OSNA’s innovative technology brings to breast cancer patients there are marked financial advantages from avoiding second surgeries and extensive post-operative analysis. Processes can be optimised and high-value resources can focus on other urgent needs. More patients can be treated during the same time saved in the theatre. Substantial bed days are saved.

- significant reduction of second surgeries
- optimised utilisation of theatre time
- reduced number of bed stays
- optimised resources
- more patients treated
- real competitive advantage for healthcare institutions

**ONE question left – or more?**

Find out about the potential savings from using OSNA in your hospital. We are able to offer an individual economic case analysis for all sites. Please consult your local representative for further details.